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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/623,596	09/05/2000	Masaaki Wachi	196811US0PCT	4864
22850	7590	12/17/2003	EXAMINER	
OBLON, SPIVAK, MCCLELLAND, MAIER & NEUSTADT, P.C. 1940 DUKE STREET ALEXANDRIA, VA 22314			KERR, KATHLEEN M	
			ART UNIT	PAPER NUMBER
			1652	

DATE MAILED: 12/17/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/623,596	WACHI ET AL.	
	Examiner	Art Unit	
	Kathleen M Kerr	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 27 August 2003.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-3,6-9 and 11-27 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☒ Claim(s) 8,9 and 11-16 is/are allowed.
- 6) ☒ Claim(s) 1-3,6,7 and 17-27 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 13) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.
- a) ☐ The translation of the foreign language provisional application has been received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Application Status

1. In response to the previous Office action, a non-Final rejection (mailed on May 27, 2003), Applicants filed an amendment received on August 27, 2003. Said amendment amended Claims 1-3, 6-9, and 18. Thus, Claims 1-3, 6-9, and 11-27 are pending in the instant Office action and will be examined herein.

Priority

2. As previously noted, the request for the benefit of priority for the International Application No. PCT/JP99/01084 filed on March 5, 1999 and the foreign application Japan 10-55608 filed on March 6, 1998, is noted. No translation of the JP document has been filed.

Drawings

3. As previously noted, the drawings have been approved by the Draftsmen and are, therefore, entered as formal drawings acceptable for publication upon the identification of allowable subject matter.

Withdrawn - Claim Objections

4. Previous objection to Claim 3 under 37 C.F.R. § 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim is withdrawn by virtue of Applicants' amendment.

Withdrawn - Claim Rejections - 35 U.S.C. § 112

5. Previous rejection of Claims 9, 12, 14, and 16 under 35 U.S.C. § 112, second paragraph, as being indefinite for the phrase “derived from” is withdrawn by virtue of Applicants’ amendment.

6. Previous rejection of Claims 9, 11, 13, and 15 under 35 U.S.C. § 112, second paragraph, as being indefinite for, in Claim 9, item a, the term “at”, is withdrawn by virtue of Applicants’ amendment.

7. Previous rejection of Claims 9, 12, 14, and 16 under 35 U.S.C. § 112, first paragraph, written description, is withdrawn by virtue of Applicants’ amendment removing the limitation of “derived from coryneform”, which subgenus did not have adequate written description.

8. Previous rejection of Claims 1, 6, 17-20, 23, and 25-27 under 35 U.S.C. § 112, first paragraph, scope of enablement, because the specification, while being enabling for methods using coryneform bacteria with a functioning PBP at particular temperatures for growth, does not reasonably provide enablement for methods coryneform bacteria without a functioning PBP at any temperature, is withdrawn by virtue of Applicants’ amendment wherein all the method claims use coryneform with a functioning PBP gene at at least one temperature.

Maintained - Claim Rejections - 35 U.S.C. § 112

9. Previous rejection of Claims 2-3, 7, 21, 22, and 24 under 35 U.S.C. § 112, second paragraph, is maintained; this rejection has been withdrawn for Claim 1 and its dependent

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claims. Applicants amended Claim 1 appropriately; however, dependent Claims 2 and 3 are now confusing in light of this amendment as follows.

The language of Claim 2 is wholly confusing, particularly in light of its dependence on Claim 1. It seems that the method is trying to distinguish two temperatures: a first temperature where the functioning PBP is produced and the mutated, native PBP is reduced/eliminated and a second temperature where the functioning PBP is not produced and the mutated, native PBP is not reduced/eliminated (i.e., is as found natively). However, Claim 1 has no optional limitation for mutating the chromosomal copy. Thus, in Claim 2, the chromosomal copy of the PBP gene **MUST** be reduced/eliminated, regardless of the temperature.

The language of Claim 3 is arduous, and lines 4-5 contain unclear limitations. The Examiner suggests simply further limiting ---the plasmid--- of Claim 1 (no other explanation, like the hybridization language, is necessary) to control expression via a temperature sensitive replication control region.

Clarification is required.

10. Previous rejection of Claims 2 and 21 under 35 U.S.C. § 112, first paragraph, written description, is maintained. Applicants' arguments have been fully considered but are not deemed persuasive for the reasons below. To reiterate, the instant rejection is set forth because "the instant claims are drawn to methods using a penicillin binding protein (PBP) gene having a temperature sensitive mutation that affects the activity of the PBP. While the specification describes using PBP genes under the control of temperature sensitive promoters, no mutation within the PBP gene is described that affects PBP activity only at certain temperatures."

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Applicants argue that the amendment limits the temperature sensitivity to the functioning PBP gene on the temperature sensitive replicon. However, due to the lack of clarity of the instant claim with respect to the nature of the PBP gene on the chromosome, the instant rejection is maintained.

11. Previous rejection of Claims 1-3, 6-7, 18-24, and 26-27 under 35 U.S.C. § 112, first paragraph, scope of enablement, because the specification, while being enabling for methods using coryneform bacteria with a reduced or eliminated PBP by virtue of a deletion, does not reasonably provide enablement for methods using coryneform bacteria with a reduced or eliminated PBP by virtue of a mutation other than deletion, is maintained. Applicants' arguments have been fully considered but are not deemed persuasive for the following reasons.

Applicants argue that a skilled artisan would be enabled to make and test mutations in the PBP genes for PBP activity of the resulting protein. However, the Examiner's point focuses on the unpredictability of such mutations to reduce or eliminate activity.

"No working examples or guidance for the non-deletion mutation of SEQ ID NO:2, or structurally similar proteins, to produce a PBP with reduced penicillin binding activity is found in the specification; all mutations are via deletion. While the state of the art is replete with examples of mutated proteins having reduced activity by virtue of a point mutation, such mutants protein-specific and cannot be correlated to the instant example without extensive information about structure relatedness. The ability to produce a reduced activity, non-deletion mutant PBP, similar to SEQ ID NO:2 is wholly unpredictable."

The lack of working examples is only one item that supports a lack of enablement. While the skilled artisan knows how to make and test mutants, no direction or predictability of which mutations to make is provided. The art offers little by way of general structure of PBP proteins so that a skilled artisan is left totally in the dark about how to make substitutions, inversions, etc.

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to produce a less active PBP. While deletion is a relatively predictable process, substitution and inversion is not. For all these reasons, the instant rejection is maintained.

12. Previous rejection of Claims 2 and 21 under 35 U.S.C. § 112, first paragraph, enablement, is maintained for the same reasons as noted above for the maintenance of the written description rejection.

Withdrawn - Claim Rejections - 35 U.S.C. § 101

13. Previous rejection of Claims 8-9 and 11-12 under 35 U.S.C. § 101 is withdrawn by virtue of Applicants' amendment.

NEW ISSUES

Claim Rejections - 35 U.S.C. § 112

The following is a quotation of the second paragraph of 35 U.S.C. § 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

14. (New) Claims 1-3, 6, 7, and 17-27 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 1 is confusing as to which chromosomal PBP gene copies are to be affected. The specification describes at least 3 PBP genes – are all of these to be mutated? Moreover, the distinction between native, non-native, functioning, and non-functioning PBP genes is unclear throughout the claims in many occurrences. This is of particular issue in Claims 17 and 19. Clarification on these points is required.

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Summary of Pending Issues

15. The following is a summary of the issues pending in the instant application:

- a) Claims 2-3, 7, 21, 22, and 24 stand rejected under 35 U.S.C. § 112, second paragraph, for being wholly confusing.
- b) (New) Claims 1-3, 6, 7, and 17-27 stand rejected under 35 U.S.C. § 112, second paragraph, as being indefinite as to the nature of the PBP gene mutated in the chromosome.
- c) Claims 2 and 21 stand rejected under 35 U.S.C. § 112, first paragraph, written description.
- d) Claims 1-3, 6-7, 18-24, and 26-27 stand rejected under 35 U.S.C. § 112, first paragraph, scope of enablement.
- e) Claims 2 and 21 stand rejected under 35 U.S.C. § 112, first paragraph, enablement.

Allowable Subject Matter

16. As previously noted, Claims 8 and 9 are considered free of the prior art. The closest prior art was noted in the previous Office action as Cole *et al.* teaching a *M. tuberculosis* gene encoding a “probably penicillin binding protein”. The structural similarities between the *M. tuberculosis* gene and SEQ ID NO:1 are outside the metes and bounds of Claims 8 and 9.

Conclusion

17. Claims 8, 9, and 11-16 are allowed; Claims 1-3, 6, 7, and 17-27 are not allowed for the reasons identified in the numbered sections of this Office action. Applicants must respond to the objections/rejections in each of the numbered sections in this Office action to be fully responsive in prosecution.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See M.P.E.P. § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 C.F.R. § 1.136(a).


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A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 C.F.R. § 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kathleen M Kerr whose telephone number is (703) 305-1229. The examiner can normally be reached on Monday through Friday, from 8:30am to 5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathupura Achutamurthy can be reached on (703) 308-3804. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 872-9306 for regular communications and (703) 872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.


PONNATHAPURA ACHUTAMURTHY
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600

Kathleen M Kerr, Patent Examiner 1652
December 4, 2003